

Company announcement

No. 24/2021

Inside information

Orphazyme A/S

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Orphazyme provides regulatory update following Type A meeting with FDA on arimoclomol in Niemann-Pick disease type C

- *Progress made in understanding potential resolution of topics outlined in Complete Response Letter, including need for additional data to support NDA*
- *FDA recommends the company provides supplemental information and analyses, and the FDA offers to have further interactions to identify a path to resubmission for arimoclomol in NPC*

Copenhagen – October 31, 2021 – Orphazyme A/S (ORPHA.CO; ORPH), a late-stage biopharmaceutical company, today provides an update on the regulatory status in the United States of its investigational product arimoclomol for Niemann-Pick disease type C (NPC) following a recently held Type A meeting with the U.S. Food and Drug Administration (FDA).

The Company had a collaborative dialogue with the FDA during the Type A meeting, which was held in order to discuss the key topics in the Complete Response Letter (CRL) issued by the FDA in June 2021. The CRL was issued based on the need for additional confirmatory evidence as well as additional qualitative and quantitative evidence to further substantiate the validity of the 5-domain NPC Clinical Severity Scale (NPCCSS), in particular the swallow domain, in the context of a lack of significant findings when using the FDA's preferred and recommended statistical approach.

The Type A meeting resulted in the following take-aways:

- The FDA recommended that the Company submit additional data, information, and analyses to address certain topics in the CRL and engage in further interactions with the FDA to identify a pathway to resubmission.
- The FDA concurred with the Company's proposal to remove the cognition domain from the NPCCSS endpoint, with the result that the primary endpoint is permitted to be recalculated using the 4-domain NPCCSS, subject to the submission of additional requested information which the Company intends to provide. To bolster the confirmatory evidence already submitted, the FDA affirmed that it would require additional in vivo or pharmacodynamic (PD)/pharmacokinetic (PK) data; the Company is considering the optimal path forward to address the FDA's requests.

"We are pleased to have gained a greater understanding from the FDA on the information that could address topics in the CRL. This is good progress. We are encouraged by the FDA's request to submit additional information and the invitation to further engage to discuss our approach and potential path forward. While we have not yet established a path to resubmission, our team will now work on putting a plan in place to discuss with the FDA during our next interactions and we will share more details about our strategy as and when appropriate" said Christophe Bourdon, Chief Executive Officer, Orphazyme A/S. He added, "We firmly believe in the establishment of a positive benefit-risk balance for arimoclomol and will continue to support the NPC community and our early access programs."

The EU Marketing Authorisation Application (MAA) for arimoclomol in NPC was filed with the European Medicines Agency in November 2020. As previously communicated, an opinion from the Committee for Medicinal Products for Human Use (CHMP) on this application is expected in Q1 2022.

For additional information, please contact:**Orphazyme A/S**

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About Niemann-Pick disease type C

Niemann-Pick disease type C (NPC) is a rare, genetic, progressively debilitating, and often fatal neurodegenerative disease. It belongs to a family known as lysosomal storage disorders and is caused by mutations leading to defective NPC protein. As a consequence, lipids that are normally cleared by the lysosome accumulate in tissues and organs, including the brain, and drive the disease pathology. We estimate the incidence of NPC to be one in 100,000 live births and the number of NPC patients in the United States and in Europe to be approximately 1,800 individuals. There are no approved treatments for NPC in the U.S.

About arimoclomol

Arimoclomol is an investigational drug candidate that amplifies the production of heat shock proteins (HSPs). HSPs can rescue defective misfolded proteins, clear protein aggregates, and improve the function of lysosomes. Arimoclomol is administered orally, and has now been studied in 10 Phase 1, four Phase 2, and three pivotal Phase 2/3 trials. Arimoclomol has received Orphan Drug Designation (ODD) for NPC in the US and EU. Arimoclomol has received Fast-Track Designation (FTD), Breakthrough Therapy Designation (BTD), and Rare Pediatric Disease Designation (RPDD) from the U.S. Food and Drug Administration (FDA) for NPC. On June 17, 2021, Orphazyme received a Complete Response Letter from the FDA regarding its New Drug Application for arimoclomol for the treatment of NPC. A marketing authorization application (MAA) for arimoclomol in NPC has been filed with the European Medicines Agency and is under review.

About Orphazyme A/S

Orphazyme is a late-stage biopharmaceutical company developing arimoclomol for Niemann-Pick disease type C (NPC). Orphazyme is headquartered in Denmark and has operations in the U.S. and Switzerland. ADSs representing Orphazyme's shares are listed on Nasdaq U.S. (ORPH) and its shares are listed on Nasdaq Copenhagen (ORPHA).

Forward-looking statement

This company announcement may contain certain forward-looking statements under the U.S. Private Securities Litigation Reform Act of 1995 and otherwise, including the next steps required to obtain regulatory approval for arimoclomol in the United States following the FDA Type A meeting and the length or time and cost required therefor, and the timing of the opinion from the CHMP. Although the Company believes its expectations are based on reasonable assumptions, all statements other than statements of historical fact included in this company announcement about future events are subject to (i) change without notice and (ii) factors beyond the Company's control. These statements may include, without limitation, any statements preceded by, followed by, or including words such as "target," "believe," "expect," "aim," "intend," "may," "anticipate," "estimate," "plan," "project," "will," "can have," "likely," "should," "would," "could", and other words and terms of similar meaning or the negative thereof. Forward-looking statements are subject to inherent risks and uncertainties beyond the Company's control that could cause the Company's actual results, performance, or achievements to be materially different from the expected results, performance, or achievements expressed or implied by such forward-looking statements, including the risks and uncertainties that are described in the Risk Factors section of the Company's Annual Report on Form 20-F for the year ended December 31, 2020 filed with the U.S. Securities and Exchange Commission (SEC) on March 2, 2021, the Company's Report on Form 6-K filed with the SEC on June 11, 2021, and other filings Orphazyme makes with the SEC from time to time. These documents are available on the "Investors & Media" section of Orphazyme's website at www.orphazyme.com. Except as required by law, the Company assumes no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.